Six-Year Clinical Experience of Pediatric Murine Typhus in Houston, TX

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BACKGROUND

- Murine typhus is a flea-borne rickettsial disease[1-3]
- Endemic to gulf states (including Houston, TX)[1-3]
- Shares clinical features of Kawasaki disease (KD) and multisystem inflammatory syndrome in children (MIS-C)[4,5]

OBJECTIVE

We explored the six-year experience with murine typhus among children living in Houston, TX. Overlap of clinical and laboratory features with KD and MIS-C were evaluated.

METHODS

- Retrospective chart review, Jan 2015-July 2021
- Children, age 0-18 years
- Cases identified by positive *Rickettsia typhi* serology:
  - Single IgG >=1:256
  - Single IgM >=1:128
  - Increase in IgG from 1:64 to 1:28 in convalescent sera
- Excluded if additional positive infectious tests

RESULTS

- 206 unique cases
  - 50.5% female
  - Median age 10 yrs

Table 1: Serologic Diagnoses

	N (%)
Initial Test Result Positive	192 (93.2)
R typhi IgG >=1:256	103 (50.0)
R typhi IgM >=1:128	167 (81.1)
Convalescent Plasma Positive	14 (6.8)

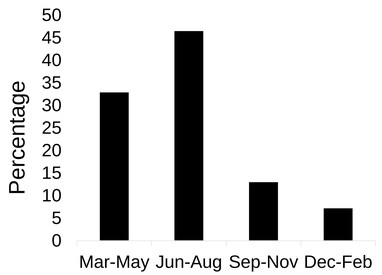
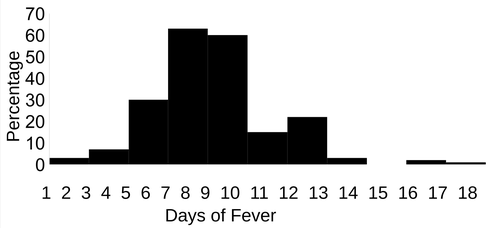


Figure 1: Seasonality of diagnosis

RESULTS (CONTINUED)

Table 2: Clinical Presentation of 206 Cases

Symptoms on Presentation	N (%)
Fever	206 (100)
Rash	144 (69.9)
Headache	131 (63.6)
Fever + Headache + Rash	**84 (40.8)**
Fatigue or Malaise	149 (72.3)
Poor Appetite	142 (68.9)
Nausea or Vomiting	117 (56.8)
Abdominal Pain	92 (44.7)
Cough	75 (36.4)
Conjunctivitis	54 (26.2)
Joint Pain	53 (25.7)
Diarrhea	51 (24.8)
Sore throat	49 (23.8)
Lymphadenopathy	18 (8.7)
Cracked Lips	17 (8.3)
Sick Contact	52 (25.2)
Exposure to SARS-CoV-2	
n/a-before February 2020	110 (53.4)
Yes	15 (7.3)
No	81 (39.3)
Documented Animal Exposures	
Dog	116 (56.3)
Cat	116 (56.3)
Opossum	26 (12.6)
Other	69 (33.5)
Documented Flea Exposure	59 (28.6)



*Mean Tmax at home = 104 °F (+/- 1.2 °F).
Mean duration of fever at home (days) = 8.8 (+/- 3.2)

Table 3: Physical Exam Findings of 206 Cases

Clinical Feature	N (%)
General Appearance	
Well-Appearing or Non-Distressed	166 (80.6)
Ill-Appearing or Distressed	33 (16.0)
Lymphadenopathy	47 (22.8)
>1.5 cm, unilateral	2 (1.0)
Conjunctivitis	41 (19.9)
Cracked, dry lips	26 (12.6)
Swelling hands and feet	2 (1.0)
Rash	116 (56.3)
Meningismus	7 (3.4)
Murmur	19 (9.3)
Abdominal Tenderness	19 (9.3)
Hepatosplenomegaly	18 (8.7)

>5 days fever + 4 KD criteria = 0
>5 days fever + 3 KD criteria = 14 (7.1%)
>5 days fever + 2 KD criteria = 29 (14.8%)

Table 4: Laboratory Findings

Laboratory Feature	Number/Sent (%)
CRP >1.0 mg/dL	181/191 (94.8)
AST>55 U/L	161/196 (82.1)
ALT>49 U/L	135/197 (68.5)
Procalcitonin >0.49 ng/mL	49/73 (67.1)
Hypoalbuminemia <3.7 g/dL	110/195 (56.4)
CK > 198 U/L	23/48 (47.9)
Thrombocytopenia <150 000 /uL	81/202 (40.0)
Hyponatremia <=133 mEq/L	47/185 (25.4)
Troponin >0.010 ng/mL	**19/75 (25.3)**
Leukocytosis >12 000 /uL	29/202 (14.4)
Lymphopenia <1000	24/202 (11.9)
BNP >100 pg/mL	**7/73 (9.6)**
Thrombocytosis >450 000 /uL	10/202 (5.0)
Leukopenia <4 000 /uL	8/202 (4.0)
Neutropenia <1500	3/202 (1.5)

Mean WBC = 8100 cells/uL (+/- 3.6); ANC = 5069 cells/uL (+/- 2901), ALC = 2418 cells/uL (+/- 1627)
Median C reactive protein = 5.6 (IQR 3.1, 8.3)

RESULTS (CONTINUED)

Table 5: Cardiothoracic Imaging

Type of Imaging	Number/Sent (%)
Abnormal Chest Radiograph*	32/130 (24.6)
Abnormal EKG**	**20/78 (25.6)**
Coronary Artery Dilation on Echocardiogram	**4/59 (6.8)**

*Focal consolidation (n=6), pleural effusion (n=6), bibasilar airspace opacities (n=3), diffuse infiltrates (n=1), and cardiomegaly (n=1)

**Diffuse ST wave abnormality (n=6), LVH (n=5), RVH (n=4), prolonged QT (n=3), T wave inversion (n=3), prolonged PR interval (n=3), and ST elevation (n=2)

Table 6: Management of 206 Cases

	N (%)
Level of Care	
Outpatient Only	20 (9.7)
ER visit	64 (31.1)
Hospitalized	122 (59.2)
Intensive care unit	17 (8.3)
Hospital Duration >48 hrs**	86/122 (70.5)
Oxygen support needed***	13/122 (10.7)
Pressor support needed	10/122 (8.2)
Treatment	
Bolus Given in ER or Hospital	101 (49.0)
Received IVIG	9 (4.4)
Received aspirin	8 (3.9)
Received remdesivir	0
Received doxycycline	183 (88.8)
5 days	8 (3.9)
7 days	73 (35.4)
10 days	54 (26.2)
14 days	9 (4.4)

**Median hospital duration (days) = 3 (IQR 2,5)
***Oxygen support included simple nasal cannula (n=7), high flow nasal cannula (n=3) BiPAP (n=1), and intubated (n=2)

CONCLUSION

- Most children were diagnosed with murine typhus in spring & summer and based on initial serological testing
- All had fever (~1 week); only 41% had classic triad of fever, HA, rash
- **Cardiac abnormalities were not uncommon**
- 4% diagnosed with KD & treated with IVIG; none during COVID-19 pandemic were diagnosed with MIS-C or acute COVID-19
- Future work: further investigate EKG & echocardiogram findings in children with murine typhus

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